UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,016	05/07/2001	Helge Voelkel	24498	3060

20529 7590 11/19/2002

NATH & ASSOCIATES
1030 15th STREET
6TH FLOOR
WASHINGTON, DC 20005

EXAMINER
SWOPE, SHERIDAN

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 11/19/2002

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,016	VOELKEL, HELGE	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *12-sept-2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22* is/are rejected.

7)☐ Claim(s) *1, 3, 11, 13, 14, 17, and 18* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election with traverse of Invention I, Claims 1-22, in Paper No. 13 is acknowledged. The traversal is on the ground(s) that, based on the International Search Report of 10-November- 2000, there is Unity of Invention for Groups I and II. This is not found persuasive. Examination, within this Office, is not restricted by the findings of International Search Reports. Invention I recites methods for screening modulators of calcineurin activity, including analysis of enzymatic activity. Wang et al, 1996 teach an enzyme assay for testing the ability of an inhibitor to overcome stabilization of calcineurin by SOD (SOD) (Fig 5) and suggest that calcineurin and SOD form a complex (Fig 1; p435 parg 2 line 18-20). Therefore, Inventions I and II do not share a novel inventive technical feature. The restriction requirement is still deemed proper and is therefore made FINAL.

Specification

The specification is objected to for numerous misspellings and improper use of appreviations. For example:

Page 9, line 9 and elsewhere: histidin should be histidine

Page 11, line 1 and elsewhere: fluoresceine should be fluorescein

Page 17, line 32 and elsewhere: bidestilled should be bidistilled

Page 18, line 14 and elsewhere: glutathion should be glutathione

Page 22, line 4 and elsewhere: splicevariants should be splice variants

NTA and SOD should be defined at their first appearance and then used throughout.

These examples are not meant to be a complete critique; a spell checker should be used.

Claim Objections

Claims 1-22 are objected to because they are replete with terms, phrases, and claim construction which lack clarity. The claims should be revised carefully in order to provide clarity.

In Claims 1, 14, and 18, and claims dependent thereon, the word enzymatical is not proper English; enzymatic is the correct word.

In Claims 1 and 3 and claims dependent thereon, "...forming of a complex..." has less clarity than "...formation of a complex...". Appropriate correction is required.

In Claim 1 and claims dependent thereon, the phrase "... under incubation with..." lacks clarity. Clarity would be provided by reciting "... in the presence of...".

The abbreviation NTA should be defined at the first appearance of nitrilotriacetat, in Claim 11, and used thereon.

Claim 13 is objected to for lack of clarity. The phrase "... in the complex formation step additionally calmodulin and/or calcium is added" is confusing and poor grammar. Clarity would be provided by using the phrase: "... in the complex formation step, calmodulin and/or calcium are present".

Claim 18 is objected to for lack of clarity. Clarity would be provided if Claim 18 was constructed to simply state that the influences of the potential modulator on the complex formation and on complex activity are analyzed separately.

Claim 17 is objected to; fluoresceine should be corrected to fluorescein.

Claim 18 is objected to; seperately should be corrected to separately.

Claim Rejections - 35 USC § 112-Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance:

Claims 1 and 18 recites the broad recitation "activity", and the claim also recites "especially the enzymatic activity" which is the narrower statement of the range/limitation.

Claim 5 recites the broad recitation "labels", and the claim also recites "especially fluorescent labels" which is the narrower statement of the range/limitation.

Claim 6 recites the broad recitation "labels", and the claim also recites "especially fluorescent marker" which is the narrower statement of the range/limitation.

Claim 6 recites the broad recitation "labels", and the claim also recites "preferably the labels are enhanced green fluorescent protein" which is the narrower statement of the range/limitation.

Claim 7 recites the broad recitation "fluorescent proteins", and the claim also recites "particularly as fusion proteins together with green fluorescent protein" which is the narrower statement of the range/limitation.

Claim 9 recites the broad recitation "cells", and the claim also recites "especially in eukaryotic cells" which is the narrower statement of the range/limitation.

Claim 10 recites the broad recitation "cells", and the claim also recites "especially in prokaryotic cells" which is the narrower statement of the range/limitation.

Claim 11 recites the broad recitation "affinity chromatography", and the claim also recites "especially by ferro-nitrilotriacetat-metal affinity chromatography" which is the narrower statement of the range/limitation.

Claim 12 recites the broad recitation "affinity chromatography", and the claim also recites "especially by copper/zinc--nitrilotriacetat-metal affinity chromatography" which is the narrower statement of the range/limitation.

Claim 15 recites the broad recitation "a label", and the claim also recites "especially a fluorescent label" which is the narrower statement of the range/limitation.

Claim 16 recites the broad recitation "peptide", and the claim also recites "especially a peptide characterized by the amino acid sequence...." which is the narrower statement of the range/limitation.

Claim 17 recites the broad recitation "a residue", and the claim also recites "especially a serine residue" which is the narrower statement of the range/limitation.

Claim 19 recites the broad recitation "method", and the claim also recites "especially according to Claim 1" which is the narrower statement of the range/limitation.

Claim 20 recites the broad recitation "tag", and the claim also recites "especially a histidine tag" which is the narrower statement of the range/limitation.

Claim 22 recites the broad recitation "a solid matrix", and the claim also recites "especially a Ni-NTA, Fe-NTA, and/or CuZn-NTA matrix" which is the narrower statement of the range/limitation.

Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "activity" in Claim 1 is an undefined term that renders Claim 1 indefinite. The specification does not provide any examples, other than measuring calcineurin enzymatic activity, for ascertaining the "activity" of the complex and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. Thus, Claim 1 fails to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Since Claims 2-22 are dependent on Claim 1, Claims 1-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Examiner's Note: For the purposes of examination, it has been assumed that analysis of potential modulators will be performed only by monitoring the effects on complex formation and calcineurin phosphatase activity.

Claims 10-12 are further rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 10, it is unclear whether calcineurin and SOD are coexpressed in the same cells or are expressed in separate cells. It is also unclear whether the complex being analyzed is being formed in vitro. An interpretation of Claim 10 is that

calcineurin and SOD are coexpressed in the same cells, that complex formation occurs in the intact cell, and only the uncomplexed calcineurin or SOD are isolated. Alternatively, Claim 10 could be interpreted as a method whereby calcineurin and SOD are expressed in different cells, that free calcineurin or SOD are isolated from the respective cells, and that complex formation occurs in vitro. Thus, Claims 10-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim 13 is further rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear when, during complex formation, calmodulin and/or calcium are added. Thus, Claim 13 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claims 19-22 are further rejected under 35 U.S.C. 112, second paragraph, being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19 recites a method according to Claim 1. However, the methods of Claim 19 fail to further limit the methods of Claim 1 as, the methods of Claim 19 are distinct from the methods of Claim 1. Since Claims 20-22 are dependent on Claim 19, Claims 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite.

Claim Rejections - 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for methods of screening for modulators of calcineurin activity in the presence of SOD as well as binding of calcineurin and SOD using the calcineurin and SOD of Examples 20-25. However, the specification is not enabling for methods of using any form of calcineurin or any form of SOD. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-22 are so broad as to encompass methods of screening for modulators using any calcineurin from any source. Claims 1, 3-20, and 22 are so broad as to encompass methods of screening for modulators using any SOD from any source. Claims 2 and 21 are so broad as to encompass methods of screening for modulators using any Cu/ZnSOD from any source. The scope of each of these claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of calcineurins and SODs broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired calcineurin activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, in this case the disclosure is limited to the human calcineurin of Examples 20-25 and the human SOD of Examples 20-25.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the Claims 1-22 which, encompass use of all calcineurins, Claims 1, 3-20, and 22 which encompass use of any SOD from any source, or Claims 2 and 21 which encompass use of any Cu/ZnSOD from any source. The specification does not support the broad scope of Claims 1-22 because the specification does not establish: (A) which species of calcineurin and SOD can be used in the methods for analyzing modulation of calcneurin/SOD activity and association, (B) regions of the proteins' structure which may be modified without effecting the activity of human calcineurin, human SOD, or human CuZnSOD; (C) the general tolerance of the activity of human calcineurin, human SOD, or human CuZnSOD, to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices of human calcineurin, human SOD, or human CuZnSOD is likely to be successful.

Thus, applicants have not provided insufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope

of the claims broadly including use of any number of calcineurin, SOD, or Cu/ZnSOD enzymes or the calcineurin and SOD of Examples 20-25 with an enormous number of amino acid modifications. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of the specific proteins having the desired utility in the claimed methods as well as the identity of the specific methods is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These claims are directed to methods of using a genera of calcineurin and SOD from any source. The specification teaches the structure of no representative species of such proteins. Moreover, the specification fails to describe any representative species of calcineurin and SOD by any identifying characteristics or properties other than the functionality of having calcineurin and SOD activity, respectively. Given this lack of description of representative species encompassed by the genera of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 9, 13-16, 18, 19, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al, 1996 (IDS). Wang et al teach that calcineurin is in a complex with another protein (Fig 1) and that said protein is SOD (Fig 5). A calcium-dependent inactivator inhibited the association of calcineurin with SOD (Fig 1). In addition, Wang et al teach a phosphatase assay for testing the ability of said inhibitor to overcome stabilization of calcineurin by a Cu/Zn SOD in the presence of Ca/calmodulin (Fig 5). The phosphatase assay uses a [^{32}P]-labeled DLDVPIPGRFDRRV[^{32}P]-SVAAE phospho-peptide as described in reference #28 of Wang et al. Wang et al further teach that said inhibitor acts by inhibiting SOD rather than by acting directly on calcineurin (pg 436, prg 2, line 9-11). Claims 1-4 recite methods for screening modulators of calcineurin enzymatic activity in the presence of SOD as well as binding with SOD. Claim 13 recites methods for screening modulators of calcineurin binding to SOD and activity in the presence of SOD and Ca/calmodulin. Claims 14-16 recite methods for screening modulators of calcineurin phosphatase activity, in the presence of SOD, using labeled substrate, especially a peptide with the sequence DLDVPIPGRFDRRVSVAAE. Claims 19 and 21 recite methods for determining the interaction of a potential calcineurin modulator with either calcineurin or SOD. Thus, Claims 1-4, 14-16, 19, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al, 1996.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al, 1996 in view of Brown et al, 1997. The teachings of Wang et al are described above. Wang et al do not teach monitoring calcineurin binding with SOD using fluorescent labels. A review of the art on the use of fluorescence-labeled proteins for assaying protein-protein interactions, including the use of laser fluctuation correlation spectroscopy, is taught by Brown et al (pg 46 parg4). Since monitoring protein-protein interaction using fluorescently-label proteins was common in the art and the teachings of Wang show that SOD binds with calcineurin (Fig 1), it would have been obvious to a person of ordinary skill in the art to test for modulators of the association between calcineurin and SOD using fluorescently-labeled proteins. Motivation to use the methods of Brown et al to screen for modulators of calcineurin is provided by the desire to determine whether modulators of calcineurin affect binding between calcineurin and SOD. The expectation of success is high as the use of fluorescently-labeled proteins to demonstrate protein-protein interaction has become standard in the art (Brown et al). Therefore, Claims 5-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al, 1996 in view of Brown et al, 1997.

Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al, 1996 in view of Woodrow et al, 1993. The teachings of Wang et al are described above. Wang et al do not teach a method for screening for modulators of calcineurin/SOD activity wherein the two proteins are coexpressed in cells. Woodrow et al teach the regulation of calcineurin in intact cells upon cotransfection with a NFAT reporter construct (Fig 1A). In addition, Woodrow et al teach that, upon coexpression, calcineurin synergizes with V-Ha-ras in intact cells to regulate NFAT (Fig 3). Since Wang et al teaches that SOD modulates the activity of calcineurin (Fig 5),

it would have been obvious to a person of ordinary skill in the art to use the method of Woodrow et al to screen for modulators of calcineurin activity upon coexpression with SOD. Motivation to so derives from the desire to identify agents that can modulate calcineurin/SOD when these two proteins are coexpressed in cells.

Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al, 1996 in view of Lau et al, 1996 or Robbins et al, 1993 and further in view of Aramburu et al, 1998. The teachings of Wang et al are described above. Wang et al do not teach purification of calcineurin prior to formation of a complex with SOD or measusrement of calcineurin activity. Lau et al teach the use of His6-tagged fusion proteins, derived from the NMDA glutamate receptor and purified with a metal-NTA column, to test interaction of the receptor with SAP102 (Fig 3). It would have been obvious to a person of ordinary skill in the art to use the method of Lau et al to prepare His6-tagged calcineurin and His6-tagged SOD, purify said proteins with a metal-NTA column, and test for binding between calcineurin and SOD using said His-tagged proteins. Use of the methods of Lau et al to prepare His6-tagged calcineurin and His6-tagged SOD and then test for binding is suggested by Wang et al. who teach that calcineurin is complexed with SOD (Fig 1). Robbins et al teach purification of recombinant his-tagged ERK2 prior to analysis for the regulation of kinase activity in vitro (Fig 7). Since Wang et al teach that association of SOD with calcineurin stabilizes the enzymatic activity of calcineurin (Figs 1 & 5), it would have been obvious to a person of ordinary skill in the art to use the method of Robbins et al, to screen for modulators of calcineurin/SOD activity using His6-tagged calcineurin and/or His6-tagged SOD. Motivation to use the methods of Robbins et al and Lau et al to test for modulators of calcineurin activity and binding between purified calcineurin and SOD,

respectively, is provided by the desire to know whether said modulators directly affect the activity and association of the calcineurin/SOD complex. The expectation of success is high as GST fusion proteins have been used to demonstrate regulation of calcineurin activity and binding with NFAT by a peptide derived from the site on NFAT that binds calcineurin (Aramburu et al; Fig 3). Therefore, Claims 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al, 1996 in view of Lau et al, 1996 or Robbins et al, 1993 and further in view of Aramburu et al, 1998.

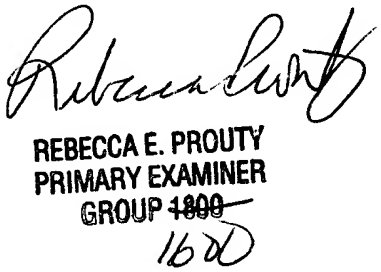
Claims 5, 15, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al, 1996 in view of admission of availability (Specification page 28 lines 21-24). Wang et al teach the use of [^{32}P]-labeled substrates but, do not teach the use of fluorescently-labeled substrates for testing the effect of potential modulators of calcineurin phosphatase activity in the presence of SOD. This specification teaches that fluorescently-labeled substrates are commercially available (page 28 lines 21-24). Motivation to use a fluorescently-tagged substrate derives from the desire to eliminate the use of radioactivity. Since Wang et al teaches that SOD regulates calcineurin activity (Fig 5), it would have been obvious to a person of ordinary skill in the art to use a fluorescently-tagged substrate to screen for modulators of calcineurin phosphatase. The expectation of success is high as, fluorescently-tagged substrates for use in phosphatase assays is commercially available (Specification page 28 lines 21-24). Therefore, Claims 5, 15, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wang et al, 1996 in view of admission of availability (Specification page 28 lines 21-24).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696. The examiner can normally be reached on M-F; 8:30-5 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan L. Swope, Ph.D.



REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~
1600